

## YOU CAN CHANGE THE WORLD To Maintain Public Trust, Manage Conflict, Counsels DeAngelis

BY RICH MCMANUS

Before she could address the need for physicians to negotiate successfully the inevitable challenges of conflict of interest, Dr. Catherine DeAngelis, editor-in-chief emerita of the *Journal of the American Medical Association*, had to deal with a cultural difficulty.

“I’ve got this laser pointer in my right hand,” she confided at the outset of her Clinical Center 2018 Distinguished Clinical Research Scholar and Educator in Residence Lecture on Feb. 14, “and in my left hand is



Dr. Catherine DeAngelis says conflict, and its management, are inevitable physician realities.

this thing that advances the slides. But I’m Italian, so how am I supposed to talk?”

DeAngelis, who is also university distinguished (“not extinguished”) service professor emerita of pediatrics at Johns

Hopkins University School of Medicine and Public Health, spoke on “Conflict of Interest in Medicine: Facts and Friction.”

Trust lies at the heart of what it means to be a medical professional, she said. It holds the entire patient-caregiver enterprise intact.

“We are all in a position of trust,” she said, “but conflict of interest is ubiquitous and inevitable for all of us. We all have [conflicts] and we need to assure that they don’t result in any harm.”

Financial conflict comes in myriad forms, she explained, from payment (where “appropriateness is key, not something beyond it”) to affiliations, consultancies, competing interests and material/financial interests.

“You can choose to be in the control group or the out-of-control group,” she quipped.

Big pharmaceutical companies have

SEE **CONFLICT**, PAGE 4

## THE FAULTS IN OUR GENES What Organ Formation, Function Tell Us About Overcoming Mutations

BY CARLA GARNETT

Why do some mutations lead to disease while others seemingly overcome injury without harm? How do some cells pinch hit for their missing or hurt comrades?

With new imaging and editing tools, scientists can see intra-cell behavior first-hand like never before and can

potentially mimic the beneficial cell actions (and limit the misdeeds) to improve the lives

SEE **STAINIER**, PAGE 6



Dr. Didier Stainier

## SHAKESPEARE SAYS Help People with Disabilities Build Social Networks

BY ERIC BOCK

Disability rights advocates have fought for accessible housing and transportation and reasonable accommodation at work and school. However, many have overlooked the need for people with disabilities to meet friends and romantic partners, said Dr. Tom Shakespeare during a Feb. 6

NICHD special lecture titled “Beyond Disability” in Lipsett Amphitheater. “You can have the job, but you all want



Dr. Tom Shakespeare



Wasn't that a mighty wind? See story, p. 12.

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**Bike to Work Day, May 18**

The NIH Bicycle Commuter Club and the Division of Amenities and Transportation Services invite you to celebrate Bike to Work Day on Friday, May 18. Join your friends and colleagues as we celebrate bicycling as an environmentally friendly, fun and healthy alternative to driving.

Beginning in March, participants can register for free at [www.biketoworkmetrodc.org](http://www.biketoworkmetrodc.org). As the event approaches, DATS will send reminders to the NIH community with updates and NIH-affiliated pit stops. But remember to enter your employer as “National Institutes of Health.”

This will help us defend our title as the employer with the most participants. Additionally, anyone who registers gets a free 2018 Bike to Work Day T-shirt (available while supplies last).



**Robust Azalea Leads Off Campus Spring**

This azalea, shown in full bloom on Feb. 28, was among the first harbingers of spring on the NIH campus, along with daffodils and crocuses. Located on the hillside between Bldgs. 31 and 15K, it is an “early blooming deciduous azalea—that is, an azalea that loses its leaves in the winter,” explained Brandon Hartz, NIH landscape architect in the Office of Research Facilities. “These deciduous types are far less commonly planted than the evergreen types that are everywhere. There are at least 20 different species of deciduous azalea and they are commonly hybridized when nursery-grown, so [the photo above] is likely a hybrid of two different species to get the best traits of both. It is a lavender flowering deciduous azalea, which is even less common since most deciduous azaleas have warmer flower tones like white, yellow or orange. Azaleas are in the rhododendron genus as well,” cautioned Hartz, “so like rhododendrons, they are prone to deer damage.”

PHOTO: RICH MCMANUS



Members of the 501st Legion pose for a photo with Isabel (I) and Lina Kerr, joined by their parents Tara and Gordon. At middle, inn residents Manuel (I) and Christina Adedeji pose with Batman. At right, Lidia Rosas, the inn’s family program coordinator, smiles with the superhero.

**Holy Comic-Con at the Inn, Batman!**

The Children’s Inn at NIH hosted Comic-Con, a celebration of comic books, on Feb. 28. Inn residents and their families met some of their favorite comic book characters, created superhero-themed art projects and watched a live musical performance of video game music. Superheroes from the Foundation 4 Heroes and Star Wars characters from the 501st Legion (a Star Wars costuming organization) mingled with residents and their families and posed for photos. The Leidos Scoop ice cream truck stopped by to provide sweet treats—even caped crusaders get hungry. The Washington Metropolitan Gamer Symphony Orchestra capped off the event with a performance of music from popular video games. The orchestra is conducted by Nigel Horne of NLM’s Information Resources Branch.



The Kerr sisters pose with heroes from Foundation 4 Heroes.

PHOTOS: P. JENNIFER FORESTER

## BODY, HEAL THYSELF

## NIDCR Symposium Explores Promise of Autotherapies

BY ROBIN LATHAM

A diverse group of scientists met recently in Lipsett Amphitheater to discuss the past, present and future of autotherapies—treatments based on the body’s natural ability to heal and protect itself. “Autotherapies: Enhancing Our Innate Healing Capacity,” hosted by the National Institute of Dental and Craniofacial Research, featured a morning of presentations from leading-edge researchers in the field.

NIDCR director Dr. Martha Somerman opened the symposium by pointing out that the meeting was a direct result of a strategic planning initiative to envision the future of NIDCR research. Five specific themes emerged from the NIDCR 2030 effort to guide the institute’s research priorities. Advancing the development of autotherapies is one of those five themes and the first to be explored via a symposium.

“The fact that we are here today discussing autotherapies is a testament to the talent and passion of NIDCR-supported dental, oral and craniofacial researchers,” said Somerman. “Over the past several decades, they’ve moved our field forward and have positioned us to be a leader in this new era of science.”

NIH principal deputy director Dr.



NIDCR director Dr. Martha Somerman opens the symposium.

Lawrence Tabak, former director of NIDCR, described the concept of autotherapies and NIH’s support of their development. Cancer immunotherapies, which harness the body’s immune system to fight malignant cells, are probably the best known autotherapies in clinical use. For example, NCI’s Dr. Steven Rosenberg and his team have pioneered immunotherapies to treat melanoma.

Presenters who followed revealed a dynamic field of inquiry in which important advances have been made, while emphasizing that further progress will require more questions to be asked and answered.

Dr. Jeffrey Karp and his team at the Harvard Stem Cell Institute have developed a therapy that uses small molecule drugs in a mouse model to reprogram noise-damaged sensory cells in the inner ear to restore hearing. A phase II study in humans is expected to begin later in 2018.

## NIDCR clinical

director Dr. Janice Lee discussed her team’s study of children’s innate ability to self-correct or regenerate a large bone defect compared to adults and noted a potential role for bone morphogenic protein, BMP6, in aging environments. She also described a study conducted by another research team on autocorrection of an *in utero* cleft palate in a mouse model using small molecule therapy with an inhibitor of Dkk1.

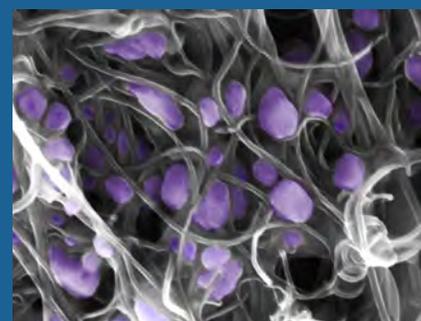
Dr. Edward Botchwey of Georgia Tech and Emory University focused on

how membrane lipidomics can be used to determine the potency of biomanufactured mesenchymal stem cells.

Dr. Robert Ferris of the University of Pittsburgh Medical Center ended the symposium with a discussion of his team’s study of the molecular pathways that allow head and neck cancer tumors to escape immune system surveillance and tactics to restore the immune system’s recognition of malignant cells.

In the final session, the panel of presenters fielded questions from the audience and engaged in a discussion on the gaps, challenges and opportunities for advancing autotherapies research.

View the archived symposium at <https://videocast.nih.gov/summary.asp?Live=26885&bhcp=1>. 



ON THE COVER: H5N2 avian influenza virus (purple) trapped in carbon nanotubes (gray mesh).

IMAGE: PENN STATE UNIVERSITY (WITH FUNDING FROM NCATS, NCI & THE NIH COMMON FUND)

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At the autotherapies symposium are (from l) Somerman; Dr. Lawrence Tabak, NIH principal deputy director; Dr. Janice Lee, NIDCR clinical director; Dr. Robert Ferris, director, Hillman Cancer Center, University of Pittsburgh Medical Center; and Dr. Jeffrey Karp, associate professor, Brigham and Women’s Hospital, Harvard Medical School. Not shown is Dr. Edward Botchwey, associate professor, Wallace H. Coulter department of biomedical engineering at Georgia Tech & Emory University, who also presented at the symposium.

PHOTOS: CHIA-CHI CHARLIE CHANG

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Turning Discovery Into Health



## Conflict

CONTINUED FROM PAGE 1

focused more in recent years on marketing than on science, she said. “The pipeline for new drugs is drying up.”

Drug companies are, of course, indispensable, DeAngelis allowed, but many relentlessly scheme for profits rather than produce new drugs.

She once studied the number of conflict-of-interest articles cited annually in PubMed, from 1974 to 2010. There was virtually nothing until the late 1980s, when the number spiked dramatically.

That was about the time that pharma CEOs were claiming that it cost about \$800 million to develop one new drug, a figure that, 2 years ago, ballooned to \$3.2 billion. Big money was prompting a shady culture of influence-peddling.

A New York skeptic in the mold of the old TV detective Columbo, DeAngelis wasn’t buying these inflated figures and demanded an explanation. When a CEO tried to insert NIH’s annual budget appropriation into the new-drug cost calculus, DeAngelis called b.s. “Sir, I was born at night, but not last night.”

From her perch as *JAMA* editor, DeAngelis and her peers at other major medical journals could detect a growing odor of corruption. Drug companies would buy the credibility of otherwise esteemed physicians, at whose talks paid audience members would encourage off-label use of the drug being touted.

“These companies spent hundreds of millions of dollars each year influencing doctors’ decisions,” said DeAngelis. “They wouldn’t do it if it weren’t effective.”

She estimates that between 1 and 2 of every 4 investigators now has an industry

★ ★ ★  
“Here we were, 12 people, with no legal jurisdiction or standing, and we made a difference. Don’t think you can’t make a change.”

-DR. CATHERINE DEANGELIS

★ ★ ★

affiliation. And studies show that pharma gets what it pays for—if a drug company funds an evaluation, you can bet its product will be “proven” effective. “Anybody who thinks it doesn’t is living in la-la land.”

Other ills catalogued by DeAngelis and her fellow editors include hiding the bad news in clinical trials, fabricating data, hiring guest authors and ghost writers who had nothing to do with the study and deliberate lying, including one paper that reported only 6 months of data when there were actually 12 months of data available.

To address the issue of transparency in reporting trial results, the National Library of Medicine, in the early 2000s, created [www.clinicaltrials.gov](http://www.clinicaltrials.gov), an online repository of clinical trials. If you got NIH funding for your study, the law required registration at the site.

But no one was enforcing the requirement, DeAngelis said, so she and the editors of 11 other major journals made a pact among themselves: if you don’t register your trial, we won’t publish your results.

“The pharmaceutical companies, I think, wanted to kill me,” DeAngelis said. At a meeting hosted by what was then known as the Institute of Medicine, the editors withstood the objections of pharma, which was crying “Restraint of trade!”

Nonsense, countered DeAngelis, there are more than 1,000 journals.

“You’re revealing industry secrets!” Nope, she said, the compounds are deliberately blinded.

At one point in the

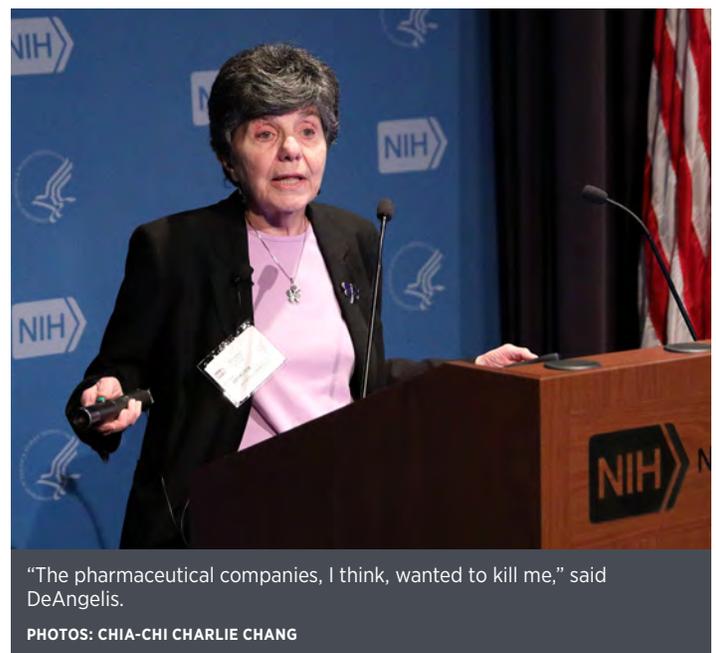
meeting, an FDA representative became indignant, charging DeAngelis and her colleagues with impeding medical progress and asking why she cared so much.

“I care because you don’t,” countered DeAngelis, “so shoot me.”

DeAngelis explains, “If they’re going to deal with my integrity, they’re going to follow my rules...Here we were, 12 people, with no legal jurisdiction or standing, and we made a difference. Don’t think you can’t make a change.”

Today, sunshine laws require all pharmaceutical and device companies to keep a record of all payments given to physicians and teaching hospitals, a step DeAngelis believes has been effective. “I know dozens of physicians and researchers who changed what they did” as a result, she said. “Policies on disclosure are essential.”

The complete talk is available at <https://videocast.nih.gov/summary.asp?Live=27082&bhcp=1>.



“The pharmaceutical companies, I think, wanted to kill me,” said DeAngelis.

PHOTOS: CHIA-CHI CHARLIE CHANG



Author Daniel Pink addresses NCI audience.

PHOTO: SHANNON CONNOLLY

## ENDINGS IMPORTANT

### Author Pink Speaks at NCI

NCI's Office of Workforce Planning and Development hosted an event with best-selling author Daniel Pink on Feb. 26.

He discussed his latest book, *When: The Scientific Secrets of Perfect Timing*, before an audience of 200 employees and fellows. The book draws on a range of scientific research in the fields of psychology, biology, economics and anthropology to illuminate the essential keys to timing our decisions and actions to thrive personally and professionally.

During his hour-long talk, Pink focused on the importance of midpoints and endings—both in life and in projects—and how to use the research about these two periods to make more informed choices and employ strategic actions.

As he explained it, productivity is often low at the beginning of a project and declines to its lowest point when the midpoint is reached. The midpoint serves as a galvanizing effect—what Pink calls “the uh-oh effect”—on both individuals and teams, often creating increased productivity as the end approaches. Pink encouraged using interim goals, which can function as artificial endpoints, to enhance productivity through a project/activity's life cycle.

Endings serve several purposes: they energize us as the end draws near, they help us encode our experience, they force us to edit and focus on what is really important and they elevate us. Yet many people discount the importance of endings. Pink encourages leaders to be thoughtful and strategic about how they end something—as the ending shapes people's entire perception of what came before.

Following his talk, Pink engaged in a 30-minute question-and-answer session with the audience and autographed copies of his book.—**Shannon Connolly**

## 100 YEARS LATER

### LaMontagne Lecturer Considers ‘Mother of All Pandemics’

Writing in his diary on Sept. 27, 1918, Charles Corning, former mayor of Concord, N.H., described how flu was blazing through his corner of the world “as fire shrivels the fields, laying out communities and taking a toll of death unprecedented.”

The next day, he observed, “A heavy sense of anxiety and apprehension like a dismal cloud in midsummer weighs heavily upon us because of the deadly ravages of the so-called Spanish influenza. Funerals jostle one another so the sable procession goes on.”

That sable procession would eventually claim 167 lives in Concord and at least 50 million more around the globe—a toll of death unmatched by any other recorded disease outbreak before or since.

This extraordinary pandemic and what scientists still can learn from it is the topic of the 2018 John Ring LaMontagne Memorial Lecture titled, “The Mother of All Pandemics and Her Naughty Children: 100 Years of Behaving Badly,” by Dr. David Morens, senior advisor to the director, NIAID. The lecture is scheduled for Tuesday, Apr. 10 at 3 p.m. in Lipsett Amphitheater, Bldg. 10.

In 2005, using preserved tissue from several 1918 flu victims, researchers determined the gene sequence of the strain of influenza A virus that sparked the pandemic and concluded that it was of avian origin. But exactly how, when and where it made the jump to humans remains unclear.

The 1918 virus was deadlier than other known flu viruses and it killed a substantial proportion of people, those ages 20 to 40, who typically survive flu infections—a phenomenon still not fully understood. Moreover, not only was the virus inherently more damaging than other influenza viruses, it had a marked ability to partner with bacteria to cause severe, often fatal, pneumonia.

Morens will describe how research on 1918 flu virus and the pandemic it caused is informing current efforts to understand how and why new flu viruses with pandemic potential emerge. He will also discuss investigations aimed at developing new and better flu vaccines, a major focus of NIAID research going into the second century of the 1918 pandemic era.

The LaMontagne lecture honors contributions to NIH and public health made by LaMontagne during his three-decade career with NIAID. He earned international recognition and widespread admiration for his distinguished leadership and accomplishments in fighting emerging and re-emerging infectious diseases. He served as NIAID deputy director from 1998 until his untimely death in 2004.—**Anne Oplinger**

APRIL 10



NIAID's Dr. David Morens



Stainier acknowledges advances in imaging technology that have benefited his research. Below, he's greeted by NCI's Dr. Kandice Tanner, who introduced the lecture.

PHOTOS: CHIA-CHI CHARLIE CHANG

## Stainier

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of people with genetic conditions.

That's according to Dr. Didier Stainier, director of the department of developmental genetics of the Max Planck Institute for Heart and Lung Research at W.G. Kerckhoff Institute in Germany. He gave a talk, "Genetic Compensation and Transcriptional Adaptation," for NCI's Center for Cancer Research Grand Rounds recently in Lipsett Amphitheater.

A longtime NIH grantee, Stainier is a "world renowned expert in elucidating mechanisms that govern organ development"—specifically heart, pancreas and liver, said Dr. Kandice Tanner, Stadtman investigator and chief of the tissue morphodynamics unit in NCI's Laboratory of Cell Biology, who introduced the speaker.

For nearly two decades, Stainier served as principal investigator on awards from NIDDK and NHLBI at the University of California, San Francisco, from 1995 to 2012.

Relocated to Germany since 2012, he and his research group use forward and reverse genetics to study the role of mutations in health and disease as various organisms—zebrafish and mice—form heart, blood vessels, pancreas, lungs and liver.

Tracing his research back to its early days, Stainier explained why he and others examine the popular aquarium fish, which belongs to the minnow family, as a vertebrate research model with potential applications to human organ development and function.

Zebrafish, he noted, are ideal for studying organ formation for several reasons, including their high fertility rate, rapid development of organs (the hearts start beating 24 hours after fertilization) and their transparency.

"One can easily see and follow the blood cells moving into and out of [the heart],"



Stainier said, showing several videos with ever-increasing definition of zebrafish hearts pumping over the past few decades, from 1990 to now. "So you can imagine how easy it was to identify mutations that affect either the form or function of this organ...It took many years and also transgenic techniques to be able to label the cardiomyocytes—the muscle cells of the heart. The imaging has been key to the various advances, not only in terms of formulating the hypotheses but also in looking at the various mutants that came out of the forward genetics screens."

• • •

## *"Why do some genetic mutations cause disease while others do not?"*

-DR. DIDIER STAINIER

• • •

It was by observing the development of hearts in zebrafish, mouse and other organisms that researchers were able to identify the heart wall's endocardium cells, watch the evolution of the cardiac pump mechanism and describe how the organ forms finger-like projections, called cardiac trabeculae, within its ventricles.

In addition to being able to map various organ structures and functions, Stainier and colleagues observed and documented other phenomena such as genetic compensation and transcriptional adaptation.

Genetic compensation, he explained, involves changes in RNA or protein levels that can functionally compensate for the loss of function of another gene. Transcriptional adaptation refers to changes in RNA levels that result from a mutation, but not from the loss of gene function.

"Transcriptional adaptation can in some cases lead to genetic compensation," Stainier added.

As a "classic illustration model" of the phenomenon, he described the genetic disorder Duchenne muscular dystrophy (DMD). DMD occurs when mutant genes obstruct proteins that build and maintain healthy muscles. In mice with DMD, the muscle-builder protein dystrophin is missing and another related muscle-builder, utrophin, goes into overdrive



For nearly 20 years, Stainier served as principal investigator on awards from NIDDK and NHLBI.

But, he explained, scientists want to fully understand how the process starts and what occurs to prompt the actions.

“The main question we had at this point is, what is the trigger for the transcriptional adaptation response?” Stainier said.

His research group tested several hypothetical prompts, finally settling on damaged or mutant RNA as the culprit. That led to more questions.

“Why do some genetic mutations cause disease while others do not?” Stainier asked. Are some mutations more or less severe than others? Also, how can more effective therapies be developed that would “enhance an organism’s robustness to a mutation rather than trying to correct the mutation?”

Investigators now are exploring ways to trigger up-regulation of the specific compensating proteins and trying to understand how the degraded mutant RNA prompts the response in the first place.

“Many black boxes remain,” Stainier concluded.

HHS’ers can access the full lecture (and previous NCI CCR Grand Rounds talks) online at <https://videocast.nih.gov/summary.asp?Live=26180&bhcp=1>. **R**

production—seemingly to make up for the lack of dystrophin.

Turns out this kind of cell behavior—up-regulation—is not uncommon.

“This phenomenon of compensation by modifier genes is not restricted to the dystrophin-utrophin model, but has been observed in many other cases of mutations for many other genes—not an isolated phenomenon by any means,” Stainier said.

Have a question about some aspect of working at NIH? You can post anonymous queries at <https://nihrecord.nih.gov/> (click on the Feedback tab) and we’ll try to provide answers.

**Feedback:** I’ve noticed that in the last few months parking on the main campus has become profoundly more difficult. Is this due to the construction work in the Bldg. 10 garage or is there another explanation? Given that we’re under a nearly complete hiring freeze, it seems unlikely that the number of employees has increased significantly. Anyway, I thought that a lot of folks on campus might be interested in knowing what’s going on.



Not an NIH lot but a somewhat-accurate representation of our recent parking crunch. Garage ramp repair, other construction projects and cold weather led to shortages, according to ORS.

PHOTO: NINJAMONKEYSTUDIO/ISTOCK

## 2nd Annual 5K Scheduled to Mark National Minority Health Month

Apr. 11

April is National Minority Health Month. On Wednesday, Apr. 11 from 11:30 a.m. to 1 p.m., join the 2nd annual Minority Health 5K Walk/Run in recognition of the month. The event will take place on the main campus in front of Bldg. 1.

Don’t forget your NIH ID and follow the walk/run at #minorityhealth5K.

NIMHD director Dr. Eliseo Pérez-Stable will give opening remarks. There will also be food trucks and music. The event is jointly sponsored by the National Institute on Minority Health and Health Disparities, the Office of Research Services and the Recreation and Welfare Association Fitness and Wellbeing Program.

Register today at <https://nimhd.nih.gov/contactform/registration-form02.html>.



Scenes from the inaugural walk/run in 2017. NIMHD director Dr. Eliseo Pérez-Stable (l) is once again set to open the event with a pep talk.

PHOTOS: CHIA-CHI CHARLIE CHANG

### Response from the Office of Research Services:

Parking on the main campus can be difficult. Recent construction on the P-2 ramp in the Bldg. 10 garage did impact parking availability as there was a temporary loss of approximately 75 parking spaces. The ramp is now open, but due to new infrastructure supports for the ramp, approximately 10 parking spaces were lost. While there has been no further loss of parking spaces, availability can be more difficult during the winter, as many NIH staff tend to commute by a single-occupied vehicle rather than by mass transit or bicycling. As the weather and Metro service improve, individuals typically switch back to mass transit or bicycling, thereby improving parking availability.

The Employee Transportation Services Office (ETSO) is here to help all NIH staff with their commuting options. We encourage you to use alternative transportation to reduce traffic and improve air quality.

If you are interested in learning about your commuter options, including transit subsidies, carpools, vanpools, bicycling or Rideshare, visit <https://www.ors.od.nih.gov/transportation>. You may also contact ETSO at [nihparkingoffice@ors.od.nih.gov](mailto:nihparkingoffice@ors.od.nih.gov) or (301) 496-5050.

## Shakespeare

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the partner and probably the family. That's a general, average human aspiration," said Shakespeare, professor of disability research at Norwich Medical School, University of East Anglia, U.K.

People with disabilities make up 15 percent of the world's population. Half of those are over 60 years old, he said. Many of them don't have the same opportunity as

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*"The internet actually liberates a lot of mobility-impaired people, a lot of deaf people, a lot of people on the autism spectrum."*

-DR. TOM SHAKESPEARE

◆ ◆ ◆  
non-disabled people to socialize with their peers.

"Most people meet their partners at college or at work. Can you get to work? Can you get to college? Are you part of that?" he asked.

For many, the answer is no. If they are in a relationship, according to U.K. research, they are twice as likely to have met their partner online. "The internet actually liberates a lot of mobility-impaired people, a lot of deaf people, a lot of people on the autism spectrum," he said.

People with disabilities—particularly those with intellectual disabilities—are perceived as "child-like and innocent." The public does not perceive people with disabilities as potential romantic partners, Shakespeare said. In some countries, they might be prevented from marrying, sterilized against their will or subjected to sexual violence.

"They don't get to have the risks, failures, the loves and the joys that most adolescents without disabilities might have," he added.

Shakespeare has followed a group of people with disabilities for the past few decades. When he first met them, they generally lacked confidence and were unhappy. As they grew older, they became emotionally stronger and saw their peers begin

to experience age-related health problems, such as a knee injury.

"Aging is good for people with disabilities," Shakespeare said, noting that others start to gain an understanding of the physical problems people with disabilities have faced all their lives. "Everybody is complaining about something or going to the hospital for something. It's not that different to what you have."

As they grow up, those with disabilities shouldn't be excluded from receiving sexual and reproductive health education, he said. Health professionals must ensure that people with disabilities have access to reproductive health services and watch closely for signs of sexual violence and abuse.

If society is going to support people with disabilities and allow them to have relationships, "we need to make sure the services we provide for them are accessible and adaptable." The problems families that are led by parents with disabilities face are often products of their social situation, not their intellectual limitations, he added.



Shakespeare and NICHD director Dr. Diana Bianchi chat with audience members at the first of two lectures he gave at NIH.

PHOTOS: ANDREW PROPP

"We must search and try to find out what they want," said Shakespeare, "and many people can indicate that with the right supports, rather than a sort of substitute decision-making, where the parent, guardian, lawyer or doctor says what's best." **R**

APRIL 23

### Krebs To Speak on Improving Chronic-Pain Management in Primary Care

Chronic pain is a complex problem with many different causes, co-occurring conditions and consequences. Primary care clinicians play a key role in caring for these patients, but research has found they face many challenges in doing so—such as workload burdens and health systems not designed or equipped for chronic-pain management.

On Monday, Apr. 23 at 11 a.m., Dr. Erin Krebs will lecture in Lipsett Amphitheater, Bldg. 10, on "Reframing the Primary Care Management of Chronic Pain." An internist, Krebs is a health-services researcher and associate professor of medicine at the University of Minnesota Medical School and the Minneapolis Veterans Affairs Health Care System. Her talk is part of NCCIH's Integrative Medicine Research Lecture Series.

Krebs will discuss the characteristics and clinical needs of patients with chronic pain, including those receiving long-term opioid therapy. She will provide examples of recent and ongoing research and explore opportunities to improve chronic-pain management, including in U.S. military and veteran populations. The lecture will be available at [videocast.nih.gov](https://videocast.nih.gov) and [facebook.com/nih.nccih](https://facebook.com/nih.nccih); more information is at <https://nccih.nih.gov/news/events/IMlectures>.



PHOTO: APRIL EILERS



On hand for the celebration were (from l) Dr. Roger Glass, FIC director; Dr. Griffin Rodgers, NIDDK director; Diane Baker, wife of the NIH director; honoree Dr. Roderic Pettigrew; and Dr. Francis Collins, NIH director.

PHOTO: RAY MACDOUGALL

## NIBIB Founding Director Pettigrew Honored at Farewell

BY CHRISTINE COOPER

Dr. Roderic Pettigrew, who retired as director of the National Institute of Biomedical Imaging and Bioengineering last fall, was honored at a farewell ceremony Mar. 1 at Stone House.

He returned to campus from his new post as chief executive officer of EnHealth, which

engineering at the Georgia Institute of Technology. He came to NIH in 2002 to take on the challenge of establishing a new organization—NIBIB—and left with a legacy as founder of the “institute of cool stuff.”

At the farewell, NIH director Dr. Francis Collins offered tribute in the form of a song to the tune of Paul Simon’s *Kodachrome*. While some in the audience may never have heard of this pre-digital film for taking pictures, it was a fitting tune to honor the

*Pettigrew came to NIH in 2002 to take on the challenge of establishing a new organization—NIBIB—and left with a legacy as founder of the “institute of cool stuff.”*

will integrate engineering into all the Texas A&M colleges within the university’s system that are part of the health care enterprise. He is also executive dean of a new engineering medicine track within the initiative called EnMed that will train medical students to invent solutions to challenging medical problems.

Prior to coming to NIH, Pettigrew was professor of radiology and medicine at Emory University and professor of

radiologist who boosted imaging and bioengineering research through the introduction of a Quantum Grant program to pursue high-risk, high-impact projects designed to solve major health care problems.

Dr. Griffin Rodgers, director of NIDDK, recalled first meeting Pettigrew in 1983, when they were both competing for a Robert Wood Johnson Foundation fellowship. Both received the award and the friendship and collegiality has lasted ever since. Rodgers

lauded Pettigrew’s “passion and competitive spirit,” which helped him then, throughout his tenure at NIH and will contribute to his success in his new endeavors.

Dr. Lawrence Tabak, NIH principal deputy director, wished “happy trails to the consummate trailblazer.” Pettigrew had started NIBIB’s Trailblazer grant for early-stage investigators in exploratory, high-impact research.

Pettigrew is recognized for his focus on early-career and young investigators and increasing the diversity of the biomedical workforce. Among his accomplishments are establishing a partnership with the Howard Hughes Medical Institute to create interdisciplinary graduate training programs and serving as NIH’s acting chief officer for scientific workforce diversity.

Pettigrew has received numerous awards for advancing bioengineering and biomedical imaging research, including being one of the few people inducted into both the National Academy of Engineering and the National Academy of Medicine (formerly the Institute of Medicine).

After trying several times to talk Pettigrew out of leaving NIH, Collins lamented that he realized that Pettigrew was “created on this planet for this position” at Texas A&M and is the person who can make the vision a reality. **R**

### Become Your Healthiest Self

Would you like to learn simple ways to prevent disease and improve your relationships, emotional well-being, physical health and surroundings?

Check out NIH’s Your Healthiest Self: Wellness Toolkits ([www.nih.gov/wellnesstoolkits](http://www.nih.gov/wellnesstoolkits)) for science-based health tips in five different areas. Each area has checklists of tips you can print for yourself or share with others. The wellness toolkits also link to dozens of NIH resources, fact sheets and articles for more information. The project was assembled by NIH’s Office of Communications and Public Liaison, OD.

For example, find out how to limit your exposure to harmful substances in your home. Get advice for managing stress and adapting to change. Or learn how friends and family can help you gain better health habits.

Good health means more than preventing and treating disease. It also means striving for well-being in all areas of your life. Small changes can add up fast. Find ways to start becoming your healthiest self.



Circuits in the brain act as an internal clock that tells us it's time to sleep, controls how long we stay asleep and, according to a new study, constantly monitors changes in external temperature and integrates that information into the neural network.

IMAGE: KNAPE/ISTOCK

## The Brain's Internal Clock Continually Takes Its Temperature

Circuits in the brain act as an internal clock to tell us it is time to sleep and to control how long we then stay asleep. A new study in flies suggests that a part of that clock constantly monitors changes in external temperature and integrates that information into the neural network controlling sleep. The NINDS-supported study was published in *Nature*.

"This study takes advantage of the powerful model system of the fly's circadian clock network to demonstrate how temperature cues from the environment are used to control the time and duration of sleep," said Dr. Janet He, program director, NINDS.

The circadian clock is a fundamental process found in nearly every living organism that coordinates sleep behavior with changes in the environment. The link between the light/dark cycle and the onset of sleep is well recognized; however, changes in temperature also appear to affect sleep patterns in humans.

"The clock discovered in flies more than 30 years ago is essentially the same one found in the human brain," said Dr. Orië Shafer, associate professor at the University of Michigan and senior author of this study. "Circadian clock studies are beautiful examples of how the fly has important things to tell us about how our bodies work."

By using a special fluorescent protein that changes from green to red when neurons fire, Shafer and his

team watched the activity of different parts of the fly brain's circadian clock while they increased or decreased the surrounding temperature. To their surprise, an area in the fly brain's circadian clock called the DN1p increased its activity when cooled and became less active when heated.

As experienced by anyone who has traveled across time zones, the circadian clock can be "reset" over time in response to new day/light cycles. The clock of flies can be retrained to new cycles of either light or temperature, so Shafer and his colleagues next looked at whether DN1p is involved in resetting the clock to a new heating/cooling cycle.

Because DN1p neurons are thought to be sleep-promoting, the researchers blocked their activity or eliminated them genetically. Both affected the flies' ability to retrain their sleep cycle in response to changes in temperature, highlighting the importance of DN1p for control of sleep behavior.

The circadian clock of larger animals and humans is also sensitive to changes in temperature, and because of their larger size, would require input from external sensory organs. The fact that, despite its small size, the fly clock also relies on temperature sensors outside the brain suggests that the findings of this study could have broad implications in the control of sleep in humans.



Scientists supported by NIH's BRAIN Initiative have discovered a high-resolution map of the wiring inside the mouse brain's thirst center that may give a glimpse into how/why humans drink.

PHOTO: JUPITERIMAGES/THINKSTOCK

## Scientists Show How the Brain May Be Wired for Drinking Fluids

Scientists have uncovered a high-resolution map of the wiring inside the mouse brain's thirst center. With these blueprints, they could trick mice into becoming light or heavy water drinkers. Moreover, they discovered a quenching circuit that knew when to tell the brain, "Stop, the body has had enough."

Supported, in part, by NIH's BRAIN Initiative, the results may also provide a glimpse into the rules that govern how the brain's circuits work.

"Bodily fluids are maintained by a delicate and tightly regulated balance of thirst and satiety," said Dr. Yuki Oka of the California Institute of Technology, senior author of the study published in *Nature*. "We genetically mapped out the neuronal circuits that tell the body when to drink."

His group studied the circuits of the lamina terminalis, the thirst center located deep inside the brain. For decades, scientists have known that three groups of neurons in this area cooperated to control drinking, and they even had clues as to which type of neurons did so. But no one had a genetically defined circuit diagram for how they did it. Nor did they completely understand how the cells tell the body to stop drinking well before the stomach fully absorbs water and other fluids.

Using genes designed to help scientists dissect brain circuits, the researchers found that opposing lines of communication running through an area of the lamina terminalis called the median preoptic nucleus may be critical players. One line was essentially responsible for telling the mice to drink while the other line told them when to stop. Both seemed to work in sequential order, relaying drinking or quenching messages from one neuron to another.

"Our results shed light on a new aspect of appetite regulation," said Oka. "It appears that the act of drinking itself sends satiety signals to the brain and these neurons act like fluid flow-meters that tell the brain when the body has had enough to drink. This circuit may be the reason why the brain knows to stop drinking well before the gut has fully absorbed all the water the animal drinks."

## Antibody Treatment May Target Viral Reservoir

After receiving a course of antiretroviral therapy for their HIV-like infection, approximately half of a group of monkeys infused with a broadly neutralizing antibody to HIV combined with an immune stimulatory compound suppressed the virus for 6 months without additional treatment, according to scientists supported in part by NIAID.

The therapy may have targeted the viral reservoir—populations of long-lived, latently infected cells that harbor the virus and that lead to resurgent viral replication when suppressive therapy is discontinued.

The new findings may inform strategies that attempt to achieve sustained, drug-free viral remission in people living with HIV.

"HIV excels at evading the immune system by hiding out in certain immune cells," said NIAID director Dr. Anthony Fauci. "The virus can be suppressed to very low levels with antiretroviral therapy, but quickly rebounds to high levels if a person stops taking medications as prescribed. The findings from this early-stage research offer further evidence that achieving sustained viral remission without daily medication might be possible. This potential application is yet another example of how the research community is using powerful, broadly

neutralizing antibodies in multiple experimental applications to protect against and treat HIV.”

“Our findings suggest that the development of interventions to activate and eliminate a fraction of the viral reservoir might be possible,” said Dr. Dan Barouch, principal investigator of the study and director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center. “Although we are still a long way off from having a cure for HIV, our data suggest a strategy for targeting the viral reservoir that can be further explored.”



Ebola virus particles (red) on a larger cell. ZMAPP, a potential treatment for Ebola, includes a cocktail of monoclonal antibodies.

IMAGE: NIAID

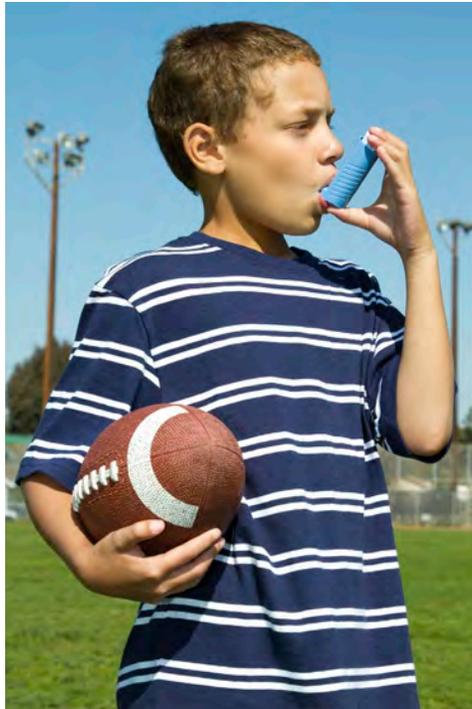
## Monoclonal Antibodies Crucial To Fighting Emerging Infectious Diseases

Monoclonal antibodies (mAbs)—preparations of a specific type of antibody designed to bind to a single target—have shown promise in the fight against cancer and autoimmune diseases. They also may play a critical role in future battles against emerging infectious disease outbreaks, according to a new article by NIAID scientists.

The article is published online by the *New England Journal of Medicine* and outlines the potential uses for mAbs as treatments for infectious diseases and as a prevention tool for protecting individuals at risk of infection and slowing disease outbreaks.

The article, written by NIAID director Dr. Anthony Fauci and colleagues Dr. Hilary Marston and Dr. Catharine Paules, highlights the research advances that could allow for rapid, strategic deployment of mAbs to prevent and treat emerging infectious diseases and, potentially, alter the course of epidemics.

Although mAbs were originally described in the 1970s, their value has become more widely recognized as scientists have developed more direct and improved approaches to identifying, selecting, optimizing and manufacturing them. These advances have allowed for improved safety and efficacy and substantial efficiencies in identifying promising candidates.



Temporarily increasing the dosage of inhaled steroids when asthma symptoms worsen does not prevent severe flare-ups.

IMAGE: CT757FAN/ISTOCK

## Increases in Inhaled Steroids Don't Prevent Asthma Flare-Ups

Researchers have found that temporarily increasing the dosage of inhaled steroids when asthma symptoms begin to worsen does not effectively prevent severe flare-ups and may be associated with slowing a child's growth. This challenges a common medical practice involving children with mild to moderate asthma.

The study, funded by NHLBI, appeared Mar. 8 in the *New England Journal of Medicine*.

Asthma flare-ups in children are common and costly. To prevent them, many health professionals recommend increasing the doses of inhaled steroids from low to high at early signs of symptoms such as coughing, wheezing and shortness of breath.

Until now, researchers had not rigorously tested the safety and efficacy of this strategy in children with mild-to-moderate asthma.

“These findings suggest that a short-term increase to high-dose inhaled steroids should not be routinely included in asthma treatment plans for children with mild-moderate asthma who are regularly using low-dose inhaled corticosteroids,” said study leader Dr. Daniel Jackson of the University of Wisconsin School of Medicine and Public Health. “Low-dose inhaled steroids remain the cornerstone of daily treatment in affected children.” **R**

## HIV Vaccine Study Needs Subjects

Vaccine Research Center scientists seek persons 18-60 years old who are living with HIV for a research study. The study evaluates an investigational product targeting the HIV virus to determine if it is safe and can generate an immune response. Compensation is provided. For more information, call 1-866-444-1132 (TTY 1-866-411-1010) or email [vaccines@nih.gov](mailto:vaccines@nih.gov). Se habla español.

## Volunteers with Leukemia Needed

NHLBI researchers need volunteers with CLL (chronic lymphocytic leukemia) or small lymphocytic lymphoma (SLL) for a new investigational treatment study. Researchers are adding pembrolizumab (an immunotherapy agent) to standard treatment. If you have received treatment for CLL and progressed or have high-risk genetic changes, such as deletion 17p, TP53 mutation, NOTCH1 mutation or complex cytogenetics, you may be interested in participating. To learn more, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more online at <https://go.usa.gov/xnYae>. Refer to study 17-H-0118.

## NIDDK Study Seeks Overweight Men

NIDDK researchers are seeking overweight/obese men, 18-50 years old, to participate in a study looking at a potential link between consumption of processed foods and the development of metabolic syndrome. Participants will be required to remain in the hospital for 1 month on 2 separate occasions and eat only the meals provided by NIH during that time. Compensation is provided. To learn more, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xRRE7>.

## Flu Vaccine Study Recruits Healthy Volunteers

Vaccine Research Center researchers seek healthy volunteers, 18-70 years old, for an investigational influenza vaccine study. Scientists are testing new vaccines to determine whether they are safe and effective in preventing the flu. Compensation is provided. For more information, call 1-866-833-5433 or email [vaccines@nih.gov](mailto:vaccines@nih.gov). Read more at <https://go.usa.gov/xNH7U>. Refer to study VRC316.

## NHLBI Study Needs Patients

NHLBI researchers are testing two low doses of danazol on individuals with short telomere disease and bone marrow disease, lung or liver disease. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xnPYm>. Refer to study 18-H-0004.



The Bethesda campus lost several trees during the Mar. 2 nor'easter, including a 32-inch diameter white pine tree (shown at left) north of the Metro Kiss and Ride, a 30-inch diameter white pine tree (c) north of MLP-7 and a 38-inch diameter white pine (below) in the east Convent courtyard; at right, other dramatic storm damage included these broken limbs from a pine tree at the security fence.

PHOTOS: PETER MOON

## Winds from 'Riley' Spank NIH Campus, Animal Center

NIH'ers woke up Friday, Mar. 2 to an alert likely never before heard affecting Washington, D.C.-area federal employees: high winds associated with a coastal nor'easter known as Winter Storm Riley—some gusting in excess of 70 m.p.h.—had closed the government for the day.

Storms have closed local federal offices before, but never due to wind alone, as far as anyone can remember. But the closure was prescient; the relentless, raking winds were responsible for downing at least 10 mature trees on the Bethesda campus, said Brandon Hartz, NIH landscape architect in the Office of Research Facilities.

These included six white pines, a hawthorn, a black locust, a slippery elm and a red maple.

"We had many other trees around campus drop large limbs," said Hartz. "In my opinion, the reason why we saw so many pines affected by the storm is that, as evergreens, they probably endured

more force from the high winds than deciduous trees that don't currently have leaves.

"As evidenced by the photos," he continued, "some of them had trunks snapped from the force of the winds. When a tree is experiencing a more gradual decline in health like disease or decay, you will often see the tree fall, but the entire tree will tip over bringing a portion of its roots and soil with it. ORF does replace dead/fallen campus trees on a yearly basis with new nursery-grown trees."

Seven cars were damaged at the Convent Dr. east parking lot, with one car left inoperable, said Peter Moon, ORF facilities program specialist.

Out at the NIH Animal Center in Poolesville, where winds roar in off the Potomac River about 30 miles northwest of Bethesda, damage from Riley was light.

"We had some perimeter security fence damage in four areas from falling trees and a couple of mature trees that blew over on campus, but did no damage," said David J. Shaw, facility manager at NIHAC. "We were fairly lucky this time."

Potentially damaging winds had been predicted days before the storm, so NIH had time to prepare. Workers flipped aluminum picnic tables upside down—to lower their risk of becoming projectiles—and in some cases chained them together.

"Tree cutting equipment was brought on campus the day before the storm, including bucket trucks, wood chippers and trucks for hauling large trees," said Moon. "Extra personnel with additional chainsaws were also added. The contractor and I were also present to assess the campus continuously before, during and after the storm. Crews were also assigned to patrol the campus during the storm to pick up any fallen debris or loose items blowing around."

Other preparations included campus-wide inspection for loose items including tables, trash bins, cigarette-butt cans and signs that needed either tightening or removal, said Reginald Stewart, chief of the Maryland Facilities Management Branch, ORF. "We also check roofs to make sure all items were secured," he added.—**Rich McManus**



Storms are not nimble enough to lay picnic tables on their backs in neat rows; this was pre-storm prep work by NIH's landscaping staff.

PHOTO: RICH MCMANUS